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Procedia Economics and Finance 38 (2016) 294 – 307

Procedia Economics and Finance

www.elsevier.com/locate/procedia

Istanbul Conference of Economics and Finance, ICEF 2015, 22-23 October 2015, Istanbul, Turkey

An Investigation of Hemophilia, Consanguineous Marriages and Economic Growth: Panel MLP and Panel SVR Approach

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Abstract

The study has two aims. The first is to investigate the interrelations of haemophilia, consanguineous marriages and their impacts on economic development. The second aim of the paper is to augment the panel regression techniques by incorporating them with Multi-Layer Perceptron neural networks models and Support Vector Machine methods. The extension is proposed to overcome the commonly criticized aspect of panel regressions, the inability to obtain homogeneity in panels. The study utilizes a panel data set that consists of 46 countries covering the 1980-2009 period and models are evaluated in terms of their ability to model the interrelations between the variables analysed. According to the empirical results, the proposed Panel Neural Network Multi-Layer Perceptron and Panel Support Vector Machine models provide success with this purpose. The empirical findings suggest that haemophilia and consanguineous marriages have significant effects on economic development.

Peer-review under responsibility of the Organizing Committee of ICEF 2015.

Keywords: Multi-layer perceptron, support vector machine, economic development, haemophilia, consanguine marriages.

1. Introduction

One point that cannot be overlooked is the fact that, though the impacts of consanguineous marriages and haemophilia have been investigated in detail by many medical and genetics papers, there is an important link among these factors and economic development. Accordingly, the paper aims at focusing on genetics in light of

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Peer-review under responsibility of the Organizing Committee of ICEF 2015.
doi:10.1016/S2212-5671(16)30203-9

consanguineous marriages and its relation to haemophilia by following an economic development perspective. Nevertheless, such diseases have strong links with social structures such as consanguineous marriages that also affect societies through its impacts on health. Further, consanguineous marriages have strong impact through human capital that also affects the economic performance of the household. Accordingly, the paper will focus on investigating consanguineous marriages, haemophilia, economic development and the relationships among them.

In clinical genetics, a consanguineous marriage means union between couples being relatives especially as the first cousins, second cousins or with a comparatively more distant relationship (Tadmouri et.al. 2009: 17-26; Grant and Bittles, 1997: 61-143). As a preferred marriage practice in some societies, this type of marriage has been a cultural practice in the Middle Eastern countries, with cousin marriages being particularly frequent among Muslim Arabs (Tamim et.al., 2003). The highest consanguineous marriage rates (from 20% to over 50% in various regions) are reported in North Africa (Bittles et al. 2001, 2002; Kanaan et al., 2008; Sathyanarayana et al., 2009).

Consanguineous marriages that had been practiced for hundreds of years in many parts of the world cause a great risk of being homozygous to a harmful gene and consequently, people practicing such marriages are subject to autosomal recessive genetic disorders, which constitute great concerns especially focusing on the children of first-degree cousins (Melki et. al., 2003). In addition, consanguineous marriages has been associated with congenital heart disease and blood diseases (haemophilia, α-thalassemia), deafness, cystic fibrosis, chronic renal failure, neonatal diabetes mellitus, prenatal and infant mortality, congenital birth defects, malformations and mental retardation, chronic renal failure, breast cancer, many genetically complex late onset diseases some autosomal recessive disorders.

Nonetheless, there is an important relationship between consanguineous marriages and haemophilia in perspectives of medical and genetics. Peyvandi et.al.(2002) discussed the occurance of bleeding disorders – such haemophilia B – and its interrelations between consanguineous marriage frequency in countries with high rates of consanguineous marriage practices such as certain middle eastern countries and southern India. Borhani et al. (2010) determined the link between frequency of bleeding disorders as a result of consanguineous marriages in family trees of African tribes. Tadmouri et.al. (2009) showed that in addition to the association of consanguineous marriages to reproductive health parameters, the main impact of consanguineous marriages is on the rate of homozygotes of recessive genetic disorders. Further, Almeida,et.al. (2002), Mansouritorgabeh et.al. (2004) and Mehdizadeh and Zamani (2008) are among the studies that evaluated the relationship between consanguineous marriages and haemophilia.

In this study, we will analyse the relationship among economic growth, consanguineous marriages and haemophilia. Since haemophilia and diseases caused by the effect of consanguineous marriage have significant implications on human capital as effectiveness and lower productivity of household, haemophilia and consanguineous marriages cause to decrease of economic growth.

The first aim of the paper is to investigate the newly proposed methods of the study; namely, the Panel Multi Layer Perceptron (MLP) and Panel Support Vector machine (SVM) analyses. The second aim of the paper is to evaluate the relationships between haemophilia, consanguineous marriages and economic development by using the proposed methods vis-à-vis the panel regressions. The Panel MLP and Panel SVM models will be discussed in Part 2. The consanguineous marriages and haemophilia is given in Part 3. Empirical analyses are given in Part 4. Part 5 concludes.

2. Panel multi-layer perceptron and panel support vector regression models

We developed two modelling techniques in this section, the Panel data Multi-Layer Perceptron (MLP) and Panel data Support Vector Machine (SVM) analyses, which are augmented nonlinear methods by deriving certain conditions from neural network learning algorithms and architectures. SVM models also possess interesting features in terms of their universal approximation properties, similar to neural networks, and the models analysed are their panel data augmentations to provide improved modelling techniques vis-à-vis the panel regression models.

2.1. Panel multi-layer perceptron (Panel-MLP)

One of the mostly applied NN models is the MLP, which is also known as the feed-forward neural network model. The MLP consists of a set of sensory units that constitute the input layer, one or more hidden layers and an output layer (Brown and Coakley, 2001). Instead of a deterministic model, we define a stochastic model with one hidden layer and with *H* hidden units. We will investigate a MLP model with panel form (Bildirici, Ersin, Kökdener, 2010),

$$\Delta y_{c,t} = \varphi\left(\alpha_{c,i} + \sum_{j=1}^{H} \beta_{c,i} I_{c,i}\left(\sum_{j=1}^{K} \gamma_{c,ij} \Delta z_{c,j,t} - \gamma_{c,i0} \right) \right) + \varepsilon_t \tag{1}$$

A simpler representation of the model is written in matrix form,

$$\mathbf{y}_{c,\mathbf{t}} = \boldsymbol{\alpha}'_{c,i} + \sum_{i=1}^{h} \beta_{c,i} I_{c,i}\left(\tilde{\boldsymbol{\omega}}', \mathbf{z}_{\mathbf{t}}, \gamma_{c,i} \right) + \varepsilon_t \tag{2}$$

activation function is defined as identity function I(x)=x where each neuron is defined as a function of $\gamma_{c,i}$ thresholds, $\mathbf{z}_{c,\mathbf{t}}$ transition variables and their weights $\tilde{\boldsymbol{\omega}}'_c$. Each neuron has a weight defined as $\beta_{c,i}$; the input vector is $\mathbf{z}_{c,\mathbf{t}} = \left(\tilde{\mathbf{z}}_{c,\mathbf{t}}, \mathbf{e}_{c,t-1}\right)'$ $\tilde{\mathbf{z}}_{c,\mathbf{t}} = \left(\mathbf{y}_{c,\mathbf{t}}, \mathbf{x}_{c,\mathbf{t}}\right)'$ where, $\mathbf{y}_{c,\mathbf{t}} = \left(\Delta y_{c,t-1},...,\Delta y_{c,t-p}\right)'$, $\mathbf{x}_{c,\mathbf{t}} = \left(\Delta x_{c,t-1},...,\Delta x_{c,t-p}\right)'$, $\mathbf{e}'_{c,t-1}$ is the error correction term. In the model, $\boldsymbol{\alpha}'_{c,i}$ is the bias term, input weights are defined as $\tilde{\boldsymbol{\omega}}'_c = \left(\boldsymbol{\delta}'_c, \boldsymbol{\eta}'_c, \boldsymbol{\kappa}'_c\right)$, where $\boldsymbol{\delta}'_c = \left(\delta_{c,1}, \delta_{c,2},.., \delta_{c,p}\right)'$, $\boldsymbol{\eta}'_c = \left(\eta_{c,1}, \eta_{c,2},.., \eta_{c,p}\right)'$, $\boldsymbol{\kappa}'_c = \left(\kappa_{c,1}, \kappa_{c,2},.., \kappa_{c,p}\right)'$. c and t is denotes country and time indices respectively. The output function φ is assumed to be linear for simplicity.

Output Weight Optimization-Hidden Weight Optimization- is an improved technique of update of the multilayer perceptron weights. Linear equations are used to solve for the output weights. Separate error functions for each hidden unit are used and multiple sets of linear equations are solved to determine the weights connecting to the hidden units.

2.2. Panel support vector regression

Support Vector Machines are learning machines developed by Vapnik (1995, 1998), Cortes and Vapnik (1992), Boser et.al. (1992) to solve pattern classification problems[†]. The approach followed in the study aims at combining SVM and ANN methodologies with panel regression models.

The support vector regression focuses on the construction of the support vector learning algorithm by mapping the original data **x** into a higher dimensional feature space *F* with the use of nonlinear mapping ϕ to obtain a linear regression space. Given a set of data $G = \left\{\left(x_i, a_i\right)\right\}_{i=1}^{N}$, where x_i is the input vector; a_i is the actual value, and *N* is the total number of data patterns, the SVM regression is stated as,

$$y = f\left(x\right) = w_i \phi_i\left(x\right) + b \tag{3}$$

[†] Certain studies followed a similar analysis to evaluate SVM and NN aproaches within a cointegration framework. İnce and Trafalis (2006) used an hybrid approach to combine SVM models with cointegration for time series data. Bildirici and Ersin (2011, 2010c) provided MLP and SVM panel cointegration methodology for panel data.

with $\phi_i : \mathrm{R}^n \to F, w \in F$. Thus, $\phi_i(x)$ is the feature of inputs x, b and w_i are the threshold and weights to be estimated by minimizing the regularized risk function,

$$R(C) = C\frac{1}{N}\sum_{i=1}^{N} L_\varepsilon(d_i, y_i) + \frac{1}{2}\|w\|^2 \tag{4}$$

and $L_\varepsilon(d_i, y_i)$ defined as,

$$L_\varepsilon(d_i, y_i) = \begin{cases} |d_i - y_i| - \varepsilon, & |d_i - y_i| \geq \varepsilon \\ 0 & otherwise \end{cases} \tag{5}$$

C and ε are prescribed parameters, d_i is the actual value and y_i is the estimation value at *i.* In the model, linear regression in a high dimensional feature space corresponds to nonlinear regression in the low dimensional input space. $L_\varepsilon(d_i, y_i)$ in Eq. (5) is the ε-insensitive loss function. The norm of w, $\frac{1}{2}\|w\|^2$ measures the flatness of the function; C represents the trade-off between the model flatness and empirical risk. Two positive slack variables ξ_i and ξ_i^* represent the distance from actual values to boundary values of the ε-tube. Soft margin computation requires the formulation of Equation (4) in the constrained form,

$$R(w, \xi_i, \xi_i^*) = \frac{1}{2}\|w\|^2 + C\left(\sum_{i=1}^{N}(\xi_i - \xi_i^*)\right) \tag{6}$$

subject to,

$$\begin{aligned} &w_i\phi_i(x) + b - d_i \leq \varepsilon + \xi_i^*, \\ &d_i - w_i\phi_i(x) - b \leq \varepsilon + \xi_i, \\ &\xi_i, \xi_i^* \geq 0 \qquad i = 1, 2, ..., N. \end{aligned} \tag{7}$$

To solve the constrained optimization problem, the following primal Lagrangian form is obtained,

$$\begin{aligned} &L(w, b, \xi, \xi^*, \alpha, \alpha^*, \beta_i, \beta_i^*) = \\ &\frac{1}{2}\|w\|^2 + C\left(\sum_{i=1}^{N}(\xi_i + \xi_i^*)\right) - \sum_{i=1}^{N}\alpha_i(w_i\phi\{x_i\} + b - d_i + \varepsilon + \xi_i) \\ &-\sum_{i=1}^{N}\alpha_i^*(d_i - w_i\phi\{x_i\} - b + \varepsilon + \xi_i^*) - \sum_{i=1}^{N}(\beta_i\xi_i + \beta_i^*\xi_i^*) \end{aligned} \tag{8}$$

The Lagrangian given in Equation (8) is minimized with respect to primal variables w, b, ξ, ξ^*; and, maximized with respect to nonnegative Lagrangian multipliers $\alpha, \alpha^*, \beta_i, \beta_i^*$. If the Kuhn-Tucker conditions are used in the regression in the regularized risk function given in Equation (4), we obtain the dual Lagrangian as,

$$J\left(\alpha,\alpha^*\right)=\sum_{j=1}^{N}d_i\left(\alpha_i-\alpha_i^*\right)-\varepsilon\sum_{j=1}^{N}\left(\alpha_i+\alpha_i^*\right)$$
$$-\frac{1}{2}\sum_{i=1}^{N}\sum_{j=1}^{N}\left(\alpha_i-\alpha_i^*\right)\left(\alpha_j-\alpha_j^*\right)K\left(x,x_t\right) \quad (9)$$

which is subject to the constraint,

$$\sum_{j=1}^{N}d_i\left(\alpha_i-\alpha_i^*\right)=0,0\le\alpha_i,\alpha_i^*\le C,i=1,2,...,N. \quad (10)$$

For the solution, first step is the calculation of α,α^* Lagrangian multipliers. In the second step, solving for w, the optimal weights of the regression is calculated:

$$w^*=\sum_{j=1}^{N}d_i\left(\alpha_i-\alpha_i^*\right)K\left(x,x_t\right). \quad (11)$$

Finally, the regression function is represented as,

$$f\left(x,\alpha_i,\alpha_i^*\right)=\sum_{j=1}^{N}d_i\left(\alpha_i-\alpha_i^*\right)K\left(x_i,x_j\right)+b^* \quad (12)$$

We have worked on SVM model with $K\left(x_i,x_j\right)$, whose value is the inner product of two *x* vectors in the ϕ feature space, $K\left(x_i,x_j\right)=\phi\left(x_i\right)\times\phi\left(x_j\right)$. Vapnik (1995) shows that any symmetric positive and semi-definite function that satisfies Mercer's conditions could be used as the Kernel functions. In SVM literature, common Kernel functions utilized are Gaussian, polynomial and linear kernel functions, which are given below:

Gaussian: $$K\left(x_i,x_j\right)=\exp\left(\left(\frac{-\left\|x_i-x_j\right\|}{2\sigma^2}\right)^2\right) \quad (13)$$

Polynomial: $$K\left(x_i,x_j\right)=\left(x_i^Tx_j+1\right)^d \quad (14)$$

Linear: $$K\left(x_i,x_j\right)=x_i^Tx_j \quad (15)$$

functions, respectively. In the study, we utilized Support Vector Regression model with linear kernel functions as a result of the purposes mentioned for MLP neural network models.

3. Haemophilia, genetics, consanguineous marriages and economic development

Haemophilia, sometimes referred to as "the royal disease", had been known since the ancient world[‡]. The first uses of the term "haemophilia" were seen in Hopff (1828) and Otto (1803)[§]. On the other hand, the earliest writings

[‡] A secondary source regarding the historical research of the sickness can be found at: http://www.hemophiliachennai.com/ancient.html

[§] Hopff was a pupil of Schönlein at the University of Zurich. His distinguished writings regarding Haemophilia is Hopff (1828), "Über die

to what appears to be haemophilia are encountered in Jewish texts of the 2nd century AD. According to Talmud, male persons having a brother being deceased after circumcision should not be circumcised. In the Babylonian version of Talmud, a story focusing on a story, which emphasizes four sisters, lived in 2nd century AD, the eldest one died after the circumcision; followed by her child's dead after the circumcision. Likewise the second and third first-born sons were subject to post-operation mortality after circumcision (tractable Yebomoth fol.64; Webb and Dixon; 1960; 143) According to other Talmud reference, Nathom was accused by a woman who had circumcised her first son, he had died and her second son, he had died. Nathan said to her, wait until his blood is absorbed, so she waited until his blood was absorbed and circumcised him and he lived (Webb and Dixon:1960;143).

Significant contributions in the literature regarding the topic could be summarized as starting from the end of the 18th and from the early 19th century. Isaac Zoll, discussed the effects of the consanguineous marriages in 1791 (qu.McKusick 1962) and others include Consbruch (1793, 1810), Rave (1796) and Otto(1803) (qu. Ingram;1976). Otto (1803) determined families with males suffered abnormalities in terms of prolonged post-traumatic bleeding. Examples were fiven from certain families: the Zoll family experienced having six brothers, all bled to death after minor injuries; in Consbruch's family, a man, Rave, and two of his sister's sons were affected, in addition to Rave, his three brothers also shown symptoms of haemophilia (Ingram;1976;469).

Otto traced back the pedigree of the family, he studied to a woman who had settled near Plymouth, New Hampshire, in about 1720. The rare occurrence of true haemophilia in the female is supposed first to have been described by Sir Frederick Treves in 1886, from a first-cousin marriage; his family was again studied by Handley and Nussbrecher in 1935, Merskey in 1951(a), Valberg in 1959, Gilchrist in 1961, and, most recently, by Kernoff and Rizza in 1973.

Haemophilia in royal families could be traced in terms of its characteristics and constituted an important source for research. Queen Victoria of England (1837–1901) was a carrier of haemophilia disease. The disease spared the majority of her children, three of her grand children and seven of her grand-grand children were affected.
If the historical occurance of haemophilia were to be investigated, the reported haemophilia prevalence among the continents of the world, the rates are highest in the European continent. Compared to other continents, Europe is followed by Asia. The prevalence of the reported haemophilia incidence show significant differences depending on the geography and time period. In the early 1970s, the prevalance of haemophilia in United Kingdom was approximately 10 persons per 100000 males versus approximately 20 per 100000 males in the United States. In 2006, the ratios are reversed – the prevalence in the United States was reported as 8.0 per 100000 males versus 20.7 per 100000 males in the United Kingdom (Stonebaker et.al., 2010)[**].

If the reported haemophilia A prevalence is evaluated among the continents, interesting results could be obtained. If heamophilia on the European continent are compared to other continents, we observe comparatively high rates in the European continent. The European continent is followed by Asian continent. The lowest levels of heamophili among continents is observed in the African continent. If analysis is done for the developed countries, China, Japan, Korea, Finland, Portugal, Germany and the United States shows a low value from the average of developed countries. In Netherlands, New Zeland, UK, Heamophilia A are the highest rates. The average for developed countries was measured as 12.36905. The relevant statistics are given for the developed countries (DC), European, African and Asian countries are given in Fig. 1.

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haemophilie oder die erbliche Anlage zu todlichen Blutungen" . For early references, see: United States Surgeon General's Catalogue, 1st series, Haemophilia (Ingram, 1976).

** The prevalence of the reported haemophilia incidence show significant differences depending on the geography and time period. In the early 1970s, the prevalance of haemophilia in United Kingdom was approximately 10 persons per 100000 males versus approximately 20 per 100000 males in the United States. In 2006, the ratios are reversed – the prevalence in the United States was reported as 8.0 per 100000 males versus 20.7 per 100000 males in the United Kingdom (Stonebaker et.al., 2010). The haemophilia prevalence is measured as the total number of reported or identified cases of haemophilia A in the population at a given time divided by the total number of males in that population.

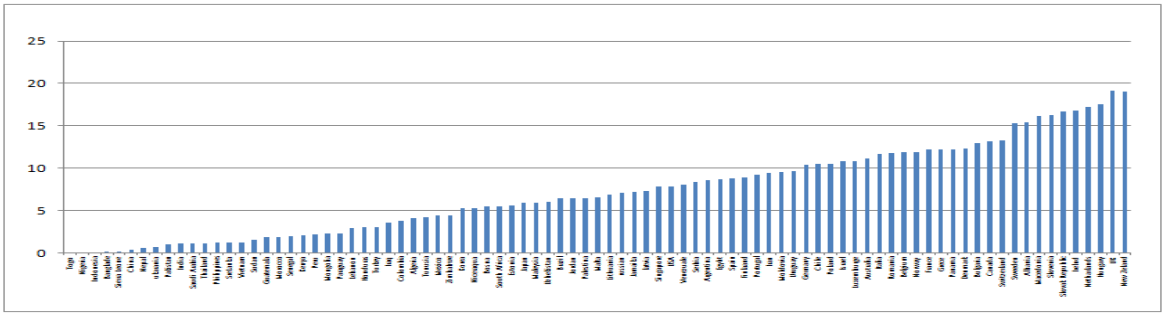

Fig. 1. Heamophilia rates, selected countries (source: given in the appendix)

As group of selected developed countries in figure 1, it is observed that the haemophilia rate ranges between 5 to 18 %; further, the majority of the observations have prevalence rates recorded in the 10-15 % range for the countries: Germany, Israel, Luxemburg, Australia, Italy, Belgium, Norway, France, Denmark, Canada and Switzerland. It should be noted that, the prevalence data has shown a changing trend in the last 2 decades. For some countries such as Canada, the rate followed an upward trend and recorded as 10.2% for Canada in 1989; as 14.2% in 2008. In Figure 1, the average of haemophilia in Europe was measured as 12.06 per 100000 males. The average of haemophilia in Asia was measured as 4,056. In Figure 5, the countries located above and below the average are evaluated. The average of haemophilia in African countries was measured as 3.271 which correspond to the lowest ratio among the other continents.

In Table 1, the relationship among haemophilia, consanguineous marriages and economic growth have several implications to be mentioned. Firstly, countries with high rate of consanguineous marriages experience comparatively low prevalence rates of haemophilia disorder in the society. Contrarily, countries practicing consanguineous marriages at with low rates experience haemophilia prevalence at high levels. At the first section of Table 1, developed countries are investigated. Compared to the countries with high consanguineous marriage practices in Asia and Africa such as Nigeria and Saudi Arabia, the developed countries given in the top rows of the Table 1 such as Austria and Germany have very low or almost no consanguineous marriage practices experience high levels of Heamophilia A prevalence rates. On the other hand, the Haemophilia A occurance in lower income countries is comparatively lower than that achieved in higher income countries. If the Haemophilia A prevalence for various lower income countries are to be evaluated we found that only 5 of 11 countries in Africa reported data on the number of people with haemophilia A with prevalence ranging from 1.7 to 6.5. On the other hand, four of nine countries in South America reported data where the prevalence ranged from 3.0 to 9.3; and only 3 of 10 countries in Asia reported data with prevalence ranging from 2.9 to 3.6 per (Stonebraker et.al., 2010).

If the relation among economic growth, consanguineous marriage and haemophilia is investigated for the countries that lowered consanguineous marriages below 10 % starting from 1980's, it is observed that haemophilia rates are relatively at high levels. Accordingly, the countries that lowered the consanguineous marriages below 10 % just before 1980 have experienced GDP growth of 4-19 folds in 23 years between 1980-2003. The GDP per capita between 1900-2003 increased for varying degrees between 0.16 and 18 fold. On the other hand, the countries that failed to lower consanguineous marriages and that maintained at 20-30% have relatively lower GDP per capita growth on the average. Among these countries, the GDP per capita grew at rates between 0.16 to 1 fold for Iran, Lebanon and Saudi Arabia. Turkey, Tunisia, Pakistan and India have increased their GDP per capita level almost 2 fold and the ratio corresponds to a very low level, if to be compared with the levels achieved by the countries that abolished consanguineous marriages in the early 19th century by the countries that dissolved it three decays ago in the early 1980's. Among these countries Haemophilia A prevalence is at relatively low level, if compared to the countries that lowered consanguineous marriages below 1% in 1900 that experienced a GDP growth of 4-19 folds between 1900-2003.

Table 1. Consanguine marriages, haemophilia and GDP per capita ratios in DC's, African and Asian countries

Countries:	*GDP per Capita ratio*		*Consanguineous Marriage Rate*	*Haemophilia A*
	2003/1900	*2003/1980*		*(Mean 1998-2006)*
Developed (European+Other)				
Austria[1]	11	6	0.01 (1988)	12
Belgium[1]	8	4	1.00 (1962)	11,9
Netherlands[1]	12	3	0.2 (1948-1952)	17,2
Finland[1]	18	5	0.012 (1989)	8,9
France[1]	12	4	0.80 (1964)	12,2
Germany[1]	10	5	3.54 (1899-1954 average)	10,4
Norway[1]	19	5	0.60 (1985)	11,9
Sweden[1]	13	3	0.60 (1953)	15,3
Switzerland[1]	11	2	0.01	13,3
United Kingdom[1]	7	3	0.40 (1980)	19,1
Irland[1]	14	7	0.60 (1991)	16,8
Spain[1]	14	8	4.10 (1979)	8,8
Australia[1]	7	3	0.50 (1966)	11,1
Canada[1]	14	3	0.06 (1991)	13,2
USA[1]	12	3	0.20 (1990)	7,8
China(a)	9	11	1.1 (1992)	0,4
Japan (a)	29	11	3.9 (1986)	5,9
Korea(a)	26	18	0 (1949/1967)	5,3
Asia				
China	9	11	1.1 (1992)	0,4
Japan	29	11	3.9 (1986)	5,9
Korea	26	18	0 (1949/1967)	5,3
Malaysia	13	5	7.6 (1966)	5,9
Singapore	32	10	5.0 (1982)	7,8
India	4	2	20-72 (1983) [3]	1,1
Iran. Islamic Rep.	8	1	31.8 (1991)	9,4
Israel	6 [2]	1	34.2 (1977)	10,8
Turkey	8	2	21.1 (1989)	3
Indonesia	5	4	17.8 (1994)	0,1
Bangladesh	1.74[2]	1.71	17.6(1976)	0,2
Pakistan	3	2	61.2 (1996)	1
Iraq	0.75	0.16	53.4 (1989)	3,6
Lebanon	1.44	0.99	21.0 (1998)	2,9
Saudi Arabia	3.39	0.57	57.7 (1995)	1,1
Africa				
Nigeria	1.79	0.95	51.2 (1974)/45.8 (1986)	0,005
Sudan	1.33	1.17	65.0 (1995)	1,6
Togo	1.08	0.57	47.6 (1996)	0,004
Jordan	6	1	63.7 (1993)	6,4
Tunisia	8	2	40.0 (1996)	4,2
Egypt	5	1	39.0 (1996)	8,7

[1]Countries in group a are also the countries that have less then 2% consang. marriage rate in 1800.
[2]As a result of the foundation in 1950's, these countries's GDP ratio is reported as GDP(2003)/GDP(1950)
[3]Different values obtained among different regions of country.
*GDP data is taken by Maddison (2003); and based on Maddison's 1990 International Geary-Khamis dollar calculations to utilize a common currency. (E)= Estimated Data, 2003/1900= 2003 per Capita GDP/1900 per Capita GDP; 2003/1950= 2003 per Capita GDP/1950 per Capita GDP 2003/1980= 2003 per Capita GDP/1980 per Capita GDP
Sources: Tadmori, O. G.(2007); Benallegue and Kedji (1984) (Algeria); ENAF (1992) (Algeria); Al-Arrayed (1999) (Bahrain); Hafez et al., (1983) (Egypt); ENPC (1989) (Egypt); Al-Hamamy et al., (1986) (Iraq); Khoury ve Massad (1992) (Jordan); Al-Nasser et al., (1989) (Kuwait); Al-Awadi et al. (1985) (Kuwait); Klat and Khudr (1986) (Lebanon); Broadhead ve Sehgal, 1981 (Libya); National Statistical Office, 1992 (Mauritania); Azelmat et al.(1987) (Morocco); Azelmat et al., 1992 (Morocco); Rajab ve Patton, 2000 (Oman); Jaber et al., 1992 (Palestine); Ministry of Health,1999 (Qatar); Wong ve Anokute, 1990 (Saudi Arabia); El-Hazmi et al., 1995 (Saudi Arabia); Saha et al., 1990 (Sudan); Prothro ve Diab, 1974 (Syria); Aloui et al., 1988 (Tunisia); Fahmy et al., 1993(UAE); Al-Gazali et al., 1995 (UAE); Jurdi ve Saxena, 2003 (Yemen); Gunaid et al., 2004 (Yemen), for Haemophilia data is compiled from Stonebaker et.al. (2010).

In the countries that failed to lower consanguineous marriages and practice it at or above 40 %, Heamophilia A patients constitute to the lowest levels among the other continents with low or almost no consanguineous marriage practices. Among African countries, the consanguineous marriage rate in Nigeria ranges between 45.8 and 51.2; whereas, the haemophilia rate is 0.005, a level very close to zero. Further, the GDP per capita ratio decreased 5 %

between 1980 and 2003. The consanguineous marriage rate in Togo is recorded as 65 %, the highest among the group and the haemophilia rate is recorded as 0.004, the lowest level among other African countries. Further, the highest level of haemophilia rate in the group of African countries is achieved as 6.4 % in Jordan with no GDP per capita growth between 1980-2003 and the consanguineous marriage rate is the second highest (63.7%) after Sudan (65%). Among the Asian countries, Iran experienced no GDP per capita increase since the GDP per capita ratio between 1980 and 2003 correspond to a value of 1.00 with consanguineous marriage ratio equal to 31.8 and haemophilia rate equal to 9.4 %. Turkey has comparatively the lowest consanguineous marriage rate (21.1 %) in the group and the lowest rate of haemophilia (3%). Egypt experiences a comparatively higher rate of haemophilia (8.7%) with consanguineous marriage rate at 39 %, above 30%, thus GDP per capita growth ratio is equal to 1, showing that there has not been GDP per capita increase on the average between 1980 and 2003. According to the data evaluated, the countries lowering consanguineous marriage rates are more likely to experience higher levels of haemophilia prevalence and GDP per capita ratio increases are highly restricted as a result of experienced low levels of health leading to distortions on the human capital in these countries.

4. Dataset and the empirical results

4.1. Data

The study covers 1980-2009 period for 46 countries which are collected under 5 country groups with respect to their consanguineous marriage. The countries included in the analysis are from various regions of the world. Austria, Belgium, Netherlands, Finland, France, Germany, Norway, Sweden, Switzerland, United Kingdom, Ireland, Australia, Canada, USA are included into Group 1. Bangladesh, India, Indonesia, Iran, Iraq, Nepal, Pakistan, Sre-Lanka, Thailand are included in Group 2. China, Japan, Korea, Maleysia, Singapore, Turkey are collected under Group 3. Nigeria, Sudan, Togo, Lebanon, Jordan, Tunisia, Egypt are collected as Group 4. Lebanon, Jordan, Tunisia, Egypt are given in Group 5. The reason behind deciding to divide the countries in the last two groups, Group 4 and 5 is the heterogeneous structure of the countries in the context of GDP. It is essential to obtain homogeneity in the panel data analysis to ensure the within group homogeneity. Panel data homogeneity tests and heteroscedasticity tests are analyzed in each group.

We utilized the haemophilia rates (HEMO= $\log(HEMO_t / HEMO_{t-1})$, the per capita GDP (LY=log per capita GDP) and consanguineous marriages (CM= log consanguineous marriages). Haemophilia data is compiled from Stonebaker et.al. (2010) and countries statistics. Per Capita GDP data is taken by Maddison (2006, 2010); and based on Maddison's 1990 International Geary-Khamis dollar calculations to utilize a common currency. The consanguineous marriage rates based on data used by Bildirici et.al. (2010a, 2010b, 2011 and 2010c). In cases where 2006 consanguineous marriage data fail to exist for a specific country, we started our search for data from 2006, year by year, towards the year 1997 which we considered to be the bottom line. We accepted the assumption that the structure of consanguineous marriage does not show a drastic change for two decays, or a generation.

4.2. Panel unit root test results

Prior to undertaking the panel MLP and Panel-SVR analysis, we performed panel unit root tests; Levin Lin Chu(LLC), Im Paseran Shin (IPS) and Fischer. Panel unit roots test results for the analysed variables are given in Table 2. The results support the hypothesis of a unit root in all variables across countries, as well as the hypothesis of zero order integration in first differences.

Table 2. Panel unit root tests

	Group 1			Group 2			Group 3		
Variable:	LLC	IPS	Fisher	LLC	IPS	Fisher	LLC	IPS	Fisher
ΔY	-13.67	-14.91	161.29	-14.83	-22.51	143.74	-12.09	-15.71	137.70
ΔCM	-48.16	-46.99	103.09	- 70.66	- 89.27	155.72	-78.94	-160.06	169.85
ΔHEMO	-20.75	-18.62	284.76	-13.48	-14.99	144.65	-38.97	-23.37	169.20
	Group 4			Group 5					
	LLC	IPS	Fisher	LLC	IPS	Fisher			
ΔY	-25.02	-15.14	69.97	-16.75	-18.86	78.59			
ΔCM	-18.27	-13.69	87.06	-12.79	-15.01	66.02			
ΔHEMO	-54.55	-10.90	134.36	-16.03	-19.20	90.12			

Notes. The unit root results represent the results for the first differenced series. *ADF - Fisher Chi-square

4.3. Panel MLP results

We estimated different Panel-MLP models for each country group. The results regarding the selected optimum neural network architecture and the learning performances are given in Table 3.

Table 3. Panel neural network models

Groups:	Architecture*	Training error**	Test error	Algorithm ***
1. Group	Panel-MLP 2-3-1	0.002368	0.003042	BFGS 44
2. Group	Panel-MLP 2-5-1	0.004697	0.006893	BFGS 105
3. Group	Panel-MLP 2-3-1	0.002264	0.002710	BFGS 75
4. Group	Panel-MLP 2-3-1	0.003811	0.004252	BFGS 37
5. Group	Panel-MLP 2-3-1	0.006528	0.005828	BFGS 17

Note: Models are estimated for 100 times for the relevant groups amounting to 500 models to be estimated with different starting values. All models have logistic (identity) activation functions in the hidden layer (output layer). Only the best models with the lowest MSE are taken to analysis as reported for each group.
*Panel MLP NN model with i-h-o architecture: i: inputs, h: no. of hidden units, o: output. All models are estimated with linear identity hidden layer and output functions. ** RMSE training and test errors. ***BFGS algorithm; the epoch number of convergence.

All Panel-MLP models have linear identity activation functions in the hidden layers. Models are estimated with BFGS learning algorithm with 75% test and 25% traning samples selected ramdomly from data. We followed the country group selections based on Table 3. We estimated 25 different Panel MLP models for each group with varying numbers of hidden neurons from 3 to 9, a minimum and maximum range selected for the number of inputs. Total number of estimated models amounted to 100 Panel-Neural-Network models with different starting values. We ranked estimated models according to the RMSE errors and selected the models with the lowest RMSE and highest generalization capability.

The correlation coefficients and the training results focusing on sensitivity analysis are given in Table 4. Accordingly, the variables included in the models are shown to be significant for the analysis of the dependent variable.

Table 4. Training performance and sensitivity of the target variable to the input variables

		Correlation coefficients		Sensitivity analysis	
Groups	Model Architecture	Train	Test	h	cm
1	Panel-MLP 2-3-1	0.92	0.90	6.39	1.91
2	Panel-MLP 2-5-1	0.95	0.94	6.36	8.04
3	Panel MLP 2-3-1	0.97	0.96	6.14	42.05
4	Panel MLP 2-3-1	0.95	0.95	269.26	61.83
5	Panel MLP 2-3-1	0.92	0.96	9.74	1.53

Inclusion of neurons further failed to improve the overall forecast capability. Therefore, we reported the most parsimonic models. Secondly, NN models are semi-parametric models. However, defined with linear or logistic activation functions and if models are parsimonic – estimated with one single hidden layer consisting of low number of hidden units, it is possible for the analyst to interpret the weights of connections between input, hidden and output layers. The weight estimates are given in Table 5.

The first model is a Panel MLP (2-3-1), two input variables, consanguineous marriage rate (cm) and heamophilia (hem); two hidden units, and the GDP per capita (ly) is the output variable. Firstly, the connections from cm to hidden neurons are estimated as -1.06277, -0.25170 and 2.26544; which suggest that the negative connection effect is larger considered in absolute terms. Hidden neron to output (per capita GDP, ly) connections are calculated as -1.06277, -0.25170 and 2.88711. To evaluate the overall effect of consanguineous marriage rate on GDP per capita, note that the parameters are estimated as -0.79691, 11.82718 and 2.26544 for cm. The overall effect is negative. Heamophilia connections are calculated as 2.20302, 2.08692 and -0.36369. The dominant effect of heamophilia increase on per capita GDP is negative for Group 1.

Table 5. Coefficient estimates of panel neural network models

No. of parameters	Weights and connections (Parameter estimates)	Group 1. Panel MLP 2-3-1	Group 2. Panel MLP 2-5-1	Group 3. Panel MLP 2-3-1	Group 4. Panel MLP 2-3-1	Group 5. Panel MLP 2-3-1
1	cm --> hidden neuron 1	-0.79691	-0.14973	-1.25868	-11.5835	-2.65237
2	cm --> hidden neuron 2	11.82718	5.94820	6.45523	2.8582	-3.33281
3	cm --> hidden neuron 3	2.26544	1.11328	-0.61173	-6.8955	-3.95732
4	cm --> hidden neuron 4		2.12779			
5	cm --> hidden neuron 5		-4.85687			
6	hem --> hidden neuron 1	2.20302	4.12989	1.87511	1.5497	-5.19200
7	hem --> hidden neuron 2	2.08692	2.88199	-3.20984	3.0466	-4.17218
8	hem --> hidden neuron 3	-0.36369	2.47024	1.94181	-0.2200	-7.26741
9	hem --> hidden neuron 4		6.47343			
10	hem --> hidden neuron 5		0.53059			
11	input bias --> hidden neuron 1	2.95778	-2.05328	1.32354	5.8110	0.21179
12	input bias --> hidden neuron 2	-1.64605	0.19262	-0.60146	2.3830	1.55130
13	input bias --> hidden neuron 3	-0.74515	-1.49507	-2.75288	-1.7538	2.12967
14	input bias --> hidden neuron 4		-3.92641			
15	input bias --> hidden neuron 5		-2.02114			
16	hidden neuron 1 --> ly	-1.06277	1.67165	3.62047	6.8605	0.66557
17	hidden neuron 2 --> ly	-0.25170	-3.09203	-2.56737	-3.6224	6.03738
18	hidden neuron 3 --> ly	2.88711	3.97990	2.89723	4.5939	-5.21794
19	hidden neuron 4 --> ly		-2.00869			
20	hidden neuron 5 --> ly		5.06331			
21	hidden bias --> ly	-0.96815	-2.14769	-1.51827	-3.1231	0.17388

*Panel MLP architecture is defined as (*j*-*n*-*y*) where *j* is the number of inputs, *n* is neurons in hidden layer, *y* is output. The sign of input *j* x the sign of neuron *n* defines the sign of certain input to output layer. **** Training and test sample Pearson rho statistic. MRSE is mean relative squared error, MRAE is mean relative absolute error.

The second model that is estimated for Group 2 has five hidden units and a 2-5-1 architecture. The connections linking cm to hidden units are calculated as 1.67165, -3.09203, 3.97990,-2.00869 and 5.06331. The connections from cm are calculated as -0.14973, 5.94820, 1.11328, 2.12779 and -4.85687. Note that, activation functions are logistic activation functions bounded between [0, 1]. Therefore, consanguineous marriage rate effects per capita GDP negatively. Further, the heamophilia rate connections are calculated as 4.12989, 2.88199, 2.47024, 6.47343 and 0.53059. Given the signs of hidden unit to output connections, we noted that heamophilia rate increases have strong positive effects on the per capita GDP.

The model estimated for Group 3 is given in the third column above with Panel MLP 2-3-1 architecture similarly to the model estimated for Group 1. The first connection, cm to hidden unit 1 is estimated as -1.25868, 6.45523 and -0.61173. Heamophilia coefficients are estimated as 1.87511, -3.20984 and 1.94181.

The fourth model that is estimated for Group 4 has third hidden units and a 2-3-1 architecture. The connections from cm to hidden neurons are estimated as -11.5835, 2.8582 and -6.8955. The heamophilia rate connections are calculated as 1.5497, 3.0466 and -0.2200. Hidden neron to output (per capita GDP, ly) connections are calculated as 6.8605, -3.6224 and 4.5939.

The last model that is estimated for Group 5 has three hidden units and a 2-3-1 architecture. The connections from cm to hidden neurons are estimated as -2.65237, -3.33281 and -3.95732. The heamophilia rate connections are calculated as -5.19200, -4.17218 and -7.26741. Hidden neron to output (per capita GDP, ly) connections are calculated as 0.66557, 6.03738 and -5.21794. Overall, the negative impacts of consanguineous marriages and haemophilia are accepted for the group.

4.4. Panel- SVR results

In Table 6, the performances of Panel-SVR models are reported for each group. Based on data, when the γ parameter is set at the default values (10), decision constants are estimated. A total of 25 Panel-SVR models are estimated for each group. The one with the lowest RMSE is reported. The Panel-SVR models estimated are non-parametric. Therefore, the estimated models will be used for generalization and forecasting performances only.

Table 6. Panel-SVR models, estimated models

Criteria	Group 1.	Group 2.	Group 3.	Group 4.	Group 5.
Kernel type:	RBF (gamma=0.50)	RBF (gamma=0.50)	RBF (gamma=0.50)	RBF (gamma=0.50)	RBF (gamma=0.50)
Decision Constant	0.395284	1.899505	0.440216	1.735509	0.292146
γ	10.000	10.000	10.000	10.000	10.000
epsilon	0.100	0.100	0.100	0.100	0.100

γ : capacity parameter.

4.4. Model comparisons

For evaluation and comparison of the Panel MLP models, certain criterias are calculated and are given in Table 7. The mean square error (MSE), mean absolute error (MAE), mean relative squared error (MRSE), mean relative absolute error (MRAE) are lowest for Group 3. Correlation coefficient as a sign of fit shows improvement for Group 3 and 4.

Table 7. Goodness of Fit Comparisons for Panel MLP

Criteria	Group 1.	Group 2.	Group 3.	Group 4.	Group 5.
Mean square error	0.020577	0.044693	0.013401	0.022302	0.014155
Mean absolute error	0.119565	0.157470	0.095849	0.113975	0.092095
Mean relative squared error	0.001130	0.004424	0.001485	0.001704	0.001309
Mean relative absolute error	0.027446	0.048255	0.031496	0.030316	0.027633
Correlation coefficient	0.914665	0.947016	0.971549	0.952071	0.930604

For evaluation and comparison purposes, similar to the Panel-MLP models, the MSE, MAE, MRSE, MRAE criteria are calculated for the Panel SVR models. The results are given in Table 8. The calculated criteria are lowest for Group 5. Correlation coefficient shows that the highest fit is obtained for Group 3 and 5.

Table 8. Goodness of fit comparisons for Panel SVR

Criteria	Group 1.	Group 2.	Group 3.	Group 4.	Group 5.
Mean square error	0.027215	0.069310	0.017811	0.070713	0.008736
Mean absolute error	0.136471	0.225288	0.106363	0.189978	0.075052
Mean relative squared error	0.001471	0.006704	0.002117	0.004319	0.000778
Mean relative absolute error	0.031203	0.067184	0.035112	0.047462	0.022155
Correlation coefficient	0.900453	0.931865	0.962010	0.863352	0.956078

One point that cannot be overlooked is the fact that RMSE, MAE and RMSE values are comparatively lower for Panel SVR models. The results show generally significant enhancement in Panel-SVR models. Additionally, though the generalization accuracy of Panel-SVR models is higher, the Panel-MLP models follow their SVR variants closely. Considering the additional advantage that has been achieved for Panel-MLP models in this study in terms of parametric modelling, the panel MLP model also benefited us in terms of evaluating the relations among the haemophilia, consanguineous marriage and economic development.

Conclusion

The study aimed at evaluating the relationships between haemophilia, consanguineous marriages and economic growth by following an economic development perspective. Further, the paper also aimed at proposing Panel SVM and Panel MLP models to augment the panel regression techniques by incorporating them with Multi-Layer Perceptron and Support Vector Machine methodologies. The extension aimed at controlling the criticized aspect of panel regressions, the inability to obtain homogeneity, and therefore, possible losses in terms of describing the relationships among variables. Accordingly, the study utilized a panel data set that consisted of 46 countries covering the 1980-2009 period to evaluate haemophilia and consanguineous marriages with emphasizing their links to economic development. According to the empirical results, the relationship between economic growth, haemophilia and consanguineous marriages could not be rejected.

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